

1058-95

### Reproducibility of High Resolution Magnetic Resonance Imaging for In Vivo Monitoring of Atherosclerotic Lesions in Humans

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**Background:** MRI allows the in-vivo sequential monitoring of human atherosclerotic lesions. The purpose of this study was to investigate the reproducibility of non-invasive MRI for in vivo quantification of human atherosclerotic lesions.

**Method:** Two consecutive independent scans of the thoracic aorta and carotid arteries were performed in 9 asymptomatic hypercholesterolemic patients. MRI was performed using high-resolution black-blood technique. Special attention was given to match MRI of the aortic (n=9) and carotid (n=7) plaques using several anatomical landmarks. Lumen area (LA), total vascular area (TVA) and vessel wall area (VWA=TVA-LA) were calculated by computer-assisted tracing of cross-sectional vessel images. The image specific error (ISE) was defined as the absolute difference in the tracing of matched images. Percentage error = (ISE/mean of 2 tracings)\*100%.

**Results: Aortic Lesions:** The mean LA was  $462 \pm 143 \text{ mm}^2$  with a VWA of  $245 \pm 66 \text{ mm}^2$ . The absolute ISE when measuring VWA was  $11 \pm 8 \text{ mm}^2$ ; however when the average measurement of 5 sections were considered, the error was markedly reduced to a  $6 \pm 4 \text{ mm}^2$  corresponding to an error of  $2.4 \pm 1.7\%$ .

**Carotid Lesion:** The mean LA was  $34 \pm 10 \text{ mm}^2$  with a VWA of  $48 \pm 18 \text{ mm}^2$ . The absolute ISE when measuring VWA was  $3 \pm 3 \text{ mm}^2$ ; however when the average measurement of 5 sections were considered, the error was markedly reduced to a  $1 \pm 1 \text{ mm}^2$  corresponding to an error of  $3.0 \pm 2.5\%$ .

Based on the reported data on reproducibility changes in plaque size of more than 5% for aortic and 7% for carotids (corresponding to 2\*SD) considering the average of 5 contiguous images for comparison, will be "real" and accurately detected by MRI.

**Conclusions:** High-resolution MRI allows the precise and reproducible assessment of human atherosclerotic lesions in vivo which is needed for monitoring sequential changes in plaque size and to study the effectiveness of different treatments (vg. lipid-lowering) in follow-up studies.

1058-96

### Atherosclerotic Plaques, Inflammation, and Thoracic Aortic Dilatation: Insights From a Population-Based Transesophageal Echocardiographic Study With Implications for Aortic Aneurysm Formation

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**Background:** We hypothesized that aortic dilatation is an atherosclerosis-related process. **Methods:** Thoracic aortic dimensions (diameters at the sinuses of Valsalva [SV], ascending aorta [AA], aortic arch and descending aorta [DA]) were measured by transesophageal echocardiography in 373 subjects (median age 66 yr, range 51-101; 52% men) participating in a population-based study (Stroke Prevention: Assessment of Risk in a Community), who were free of significant aortic valve disease. The associations between aortic atherosclerotic plaques, markers of inflammation (high-sensitivity C-reactive protein [hs-CRP] and fibrinogen) and aortic dimensions were examined. **Results:** Age, male gender and body surface area (BSA) were significant determinants of aortic diameters. Adjusting for these variables: 1) Thick plaques in the AA (greater or equal to 4 mm) were negatively associated with SV diameter ( $P=0.03$ ); AA plaques were not associated with AA diameter; 2) The presence of aortic arch plaques (of any degree) and thick arch plaques (greater or equal to 4 mm) were associated with increased arch diameter ( $1.41 \text{ mm}$  increase in diameter [ $\pm 0.53$ ] in the presence of plaques,  $P=0.007$ ;  $2.18 \text{ mm}$  increase in diameter [ $\pm 1.11$ ] in the presence of thick plaques,  $P=0.05$ ); 3) The presence of DA plaques and greater DA plaque thickness were associated with increased DA diameter ( $1.51 \text{ mm}$  increase in diameter [ $\pm 0.53$ ] in the presence of plaques,  $P=0.004$ ;  $0.18 \text{ mm}$  increase in diameter [ $\pm 0.08$ ] per mm increase in plaque thickness,  $P=0.03$ ). Adjusting for age, gender, BSA and smoking status, hs-CRP and fibrinogen were not significantly associated with aortic dimensions (all  $P$  values  $>0.05$ ). **Conclusions:** Aortic atherosclerotic plaques are associated with distal, but not proximal, aortic dilatation. These findings support the hypothesis that atherosclerotic weakening of the vessel wall plays a role in aortic dilatation and, possibly, in aortic aneurysm formation. Systemic inflammatory markers are not associated with aortic dimensions, suggesting that non-inflammatory atherosclerotic processes are involved in aortic dilatation.

## POSTER SESSION

### 1059 Metabolic Syndrome

Sunday, March 17, 2002, 3:00 p.m.-5:00 p.m.

Georgia World Congress Center, Hall G

Presentation Hour: 3:00 p.m.-4:00 p.m.

1059-73

### Fasting Blood Glucose in the Nondiabetic Range Is a Continuous and Graded Risk Factor for CHD

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**Background:** Diabetes mellitus (DM) and impaired glucose tolerance are associated with several CHD risk factors (RF's) and a  $>2$  fold risk for CHD. Few data exist on whether glucose levels in the non-diabetic range are associated with risk for CHD when adjusted for multiple risk factors. **Objective:** We studied the relationships among fasting blood glucose (FBG)  $<126 \text{ mg/dL}$ , prevalent CHD, traditional CHD RF's (obesity, dyslipidemia, BP), Framingham risk score and non-traditional CHD RF's (Lp(a), fibrinogen, homocysteine (tHcy)) in 2440 consecutive patients without known DM at high risk for CHD in a Preventive Cardiology Clinic. **Results:** There was a trend toward increasing values across glucose quintiles for age ( $P<0.001$ ), BMI ( $P<0.001$ ), systolic BP ( $P<0.001$ ), fibrinogen ( $P<0.001$ ), tHcy ( $P<0.001$ ). There was a trend for decreasing values for HDL-c ( $P<0.001$ ), as well as for % current smokers ( $P=0.02$ ) and Lp(a) ( $P<0.001$ ). The prevalence of CHD, Framingham risk score and odds ratio (OR) for CHD risk whether unadjusted, adjusted for traditional RF's or adjusted for Framingham risk score plus non-traditional RF's is significant for the top 3 quintiles compare to the lowest (Table). **Conclusions:** FBG levels in the non-diabetic range are associated with several traditional risk factors for CHD (age, BMI, BP, HDL-c) as well as fibrinogen and tHcy. The OR for CHD increases as a continuous function of glucose whether unadjusted or fully adjusted for RF's.

\* $p<0.001$

Glucose Quintile	I	II	III	IV	V	P
FBG (mg/dL)	$\leq 79$	80-86	87-92	93-99	100-125	$<0.001$
CHD (%)	43	47	53	56	65	$<0.001$
Framingham Risk Score	4.4	5.0	5.3	5.5	6.3	$<0.001$
OR (Adjusted all risk factors)	1.0	1.16	1.52*	1.80*	2.78	$<0.001$

1059-74

### Impact of Fluvastatin Slow-Release on Low-Density Lipoprotein Subfractions in Patients With Type 2 Diabetes: Baseline Low-Density Lipoprotein Profile Determines Specific Mode of Action

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**Background:** Patients with type 2 diabetes have an increased coronary artery disease risk and lipid metabolism characterized by increased triglycerides, decreased high-density lipoprotein (HDL) cholesterol, and slightly elevated low-density lipoprotein (LDL) cholesterol. They also have a preponderance of atherogenic dense LDL (dLDL). We therefore studied the effect of slow-release (XL) fluvastatin on LDL subfractions in 89 patients with type 2 diabetes.

**Methods:** After a 4-week dietary run-in period, this multicenter, double blind, randomized, parallel-group study compared fluvastatin XL 80 mg ( $n=42$ ) with placebo ( $n=47$ ), given once daily for 8 weeks to patients (mean age: 67 years; range: 39-89 years) with mean baseline triglyceride, LDL cholesterol, and HDL cholesterol levels of 211, 154, and 44.6 mg/dL, respectively. Lipoproteins were isolated by sequential preparative ultracentrifugation and total LDL was separated into 6 subfractions by equilibrium density gradient ultracentrifugation.

**Results:** Fluvastatin decreased mean baseline LDL cholesterol ( $-32\%$ ,  $p<0.001$ ), triglycerides ( $-18\%$ ,  $p<0.001$ ), and dLDL (LDL-5:  $-27\%$ ,  $p<0.001$  and LDL-6:  $-22\%$ ,  $p<0.001$ ), these changes being statistically significant compared with placebo. The HDL cholesterol increase ( $3.1\%$ ) was not significant, but reached  $+18\%$  in patients with a baseline HDL below 35 mg/dL ( $n=10$ ). A baseline dLDL preponderance (apoB in LDL-5 + LDL-6  $>25 \text{ mg/dL}$ ) was present in 3/4 of patients. In these patients, fluvastatin decreased all LDL subfractions significantly from baseline (13.7-29.3%), absolute and relative reductions in dLDL being greatest. In patients with no baseline dLDL (apoB in LDL-5 + LDL-6  $<25 \text{ mg/dL}$ ) only LDL-1 to LDL-3 were significantly reduced, dLDL remaining unchanged.

**Conclusions:** Fluvastatin 80 mg XL effectively lowers LDL cholesterol, triglycerides, and dLDL in patients with type 2 diabetes. Fluvastatin also decreases specifically those LDL-subfractions that are increased in type 2 diabetes, with or without a predominance of dLDL. The antiatherogenic potential of fluvastatin in patients with type 2 diabetes may thus be greater than expected from its effects on LDL cholesterol and triglycerides alone.

1059-75

### Effect of Simvastatin on Insulin Resistance and Beta Cell Function in Hypercholesterolemic Patients

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**Background:** The effects of statins on insulin resistance (IR) and  $\beta$  cell function ( $\beta$ cf) are not clearly determined.

**Methods:** Hypercholesterolemic 113 patients (cholesterol level  $>200 \text{ mg/dL}$ , mean age  $53.1 \pm 13.5$  years) were studied to assess the effect of simvastatin. They were divided in